

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ABL-012-PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below	
International application No. PCT/BE 03/00192	International filing date (day/month/year) 07/11/2003	(Earliest) Priority Date (day/month/year) 08/11/2002
Applicant ABLYNX N.V.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

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Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to polypeptides derived from single domain heavy chain antibodies directed to Tumor Necrosis Factor-alpha. It further relates to single domain antibodies that are Camelidae VHVs. It further relates to methods of administering said polypeptides.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07K16/28	C07K16/18	C07K16/46	A61K39/395	C12N15/13
	G01N33/577	A61P37/06	A61P19/02		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91/02078 A (PEPTIDE TECHNOLOGY LTD) 21 February 1991 (1991-02-21) page 3, line 28 -page 4, line 24 page 15, line 25 - line 33	1
Y	---	2-49
Y	ELS CONRATH K ET AL: "Camel single-domain antibodies as modular building units in bispecific and bivalent antibody constructs" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 276, no. 10, 9 March 2001 (2001-03-09), pages 7346-7350, XP002248402 ISSN: 0021-9258 the whole document ---	2-49
	-/-	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

7 May 2004

14/05/2004

Name and mailing address of the ISA

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Le Flao, K

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VALLE E ET AL: "Infliximab" EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY, LONDON,, GB, vol. 2, June 2001 (2001-06), pages 1015-1025, XP002965315 ISSN: 1465-6566 the whole document ---	1-49
Y	WO 02/057445 A (MURUGANANDAM ARUMUGAM ;STANIMIROVIC DANICA (CA); NARANG SARAM (CA)) 25 July 2002 (2002-07-25) page 18, line 29 -page 47, line 18 ---	1-49
A	WO 02/079781 A (ANDREWS JANET S ;HESKA CORP (US); JENSEN WAYNE A (US); MCDONALD TH) 10 October 2002 (2002-10-10) page 26, line 25 -page 28, line 21 page 29, line 14 - line 20 ---	4
A	TANHA J ET AL: "Selection by phage display of llama conventional VH fragments with heavy chain antibody VHH properties" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER, AMSTERDAM, NL, vol. 263, no. 1-2, 1 May 2002 (2002-05-01), pages 97-109, XP004354388 ISSN: 0022-1759 the whole document ---	1-49
A	D'HAENS G ET AL: "ENDOSCOPIC AND HISTOLOGICAL HEALING WITH INFILIXIMAB ANTI-TUMOR NECROSIS FACTOR ANTIBODIES IN CROHN'S DISEASE: A EUROPEAN MULTICENTER TRIAL" GASTROENTEROLOGY, SAUNDERS, PHILADELPHIA, PA,, US, vol. 116, no. 5, May 1999 (1999-05), pages 1029-1034, XP009009036 ISSN: 0016-5085 the whole document -----	1-47

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 22-24

Present claims 22-24 relate to a product defined by reference to a desirable characteristic or property, namely "an unknown agent that modulates the binding of an anti-TNF-alpha polypeptide of any of claims 1 to 11, and 13 to 16 to Tumor Necrosis Factor-alpha" (claim 22) and "an unknown agent that modulates Tumor Necrosis Factor-alpha-mediated disorders" (claim 23). The scope of claims 22-24 is unclear and speculative within the meaning of Article 6 PCT. Said claims lack indication concerning their technical features. The available experimental data actually relate to anti-TNF-alpha single domain antibodies and their preparation, but not to an agent that modulates their binding. Consequently no search has been carried out for the claims 22-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: 22-24 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9102078	A	21-02-1991	AU	640400 B2	26-08-1993
			AU	6145490 A	11-03-1991
			WO	9102078 A1	21-02-1991
			EP	0486526 A1	27-05-1992
			CA	2064915 A1	08-02-1991
			DE	69027121 D1	27-06-1996
			DE	69027121 T2	14-11-1996
			DK	486526 T3	24-06-1996
			JP	3443119 B2	02-09-2003
			JP	2003096096 A	03-04-2003
			JP	2003231699 A	19-08-2003
			US	2003162948 A1	28-08-2003
			US	2003232970 A1	18-12-2003
			US	2004002588 A1	01-01-2004
			US	2003171553 A1	11-09-2003
			US	2003166874 A1	04-09-2003
			US	2003216552 A1	20-11-2003
			US	2004002589 A1	01-01-2004
			US	2003208047 A1	06-11-2003
			US	5644034 A	01-07-1997
			US	2003171554 A1	11-09-2003
			US	2003171555 A1	11-09-2003
			US	2004002590 A1	01-01-2004
			US	2003225254 A1	04-12-2003
			US	6416757 B1	09-07-2002
			US	2003232971 A1	18-12-2003
			US	6593458 B1	15-07-2003
			US	2001018507 A1	30-08-2001
			US	2001023287 A1	20-09-2001
			US	2001018508 A1	30-08-2001
WO 02057445	A	25-07-2002	AU	6885501 A	03-12-2001
			WO	0190190 A2	29-11-2001
			WO	02057445 A1	25-07-2002
			CA	2380443 A1	29-11-2001
			CA	2441903 A1	25-07-2002
			EP	1328626 A1	23-07-2003
			US	2003190598 A1	09-10-2003
WO 02079781	A	10-10-2002	CA	2442074 A1	10-10-2002
			EP	1384075 A1	28-01-2004
			WO	02079781 A1	10-10-2002
			US	2003022262 A1	30-01-2003

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